

---

**A mitochondrial etiology of Alzheimer and Parkinson disease.**

**Journal:** Biochim Biophys Acta

**Publication Year:** 2011

**Authors:** P Coskun, J Wyrembak, S Schriener, H W Chen, C Marciniack, F Laferla, D C Wallace

**PubMed link:** 21871538

**Funding Grants:** The Dangers of Mitochondrial DNA Heteroplasmy in Stem Cells Created by Therapeutic Cloning

**Public Summary:**

**Scientific Abstract:**

**BACKGROUND:** The genetics and pathophysiology of Alzheimer Disease (AD) and Parkinson Disease (PD) appears complex. However, mitochondrial dysfunction is a common observation in these and other neurodegenerative diseases. **SCOPE OF REVIEW:** We argue that the available data on AD and PD can be incorporated into a single integrated paradigm based on mitochondrial genetics and pathophysiology. **MAJOR CONCLUSIONS:** Rare chromosomal cases of AD and PD can be interpreted as affecting mitochondrial function, quality control, and mitochondrial DNA (mtDNA) integrity. mtDNA lineages, haplogroups, such haplogroup H5a which harbors the mtDNA tRNA(Gln) A8336G variant, are important risk factors for AD and PD. Somatic mtDNA mutations are elevated in AD, PD, and Down Syndrome and Dementia (DSAD) both in brains and also systemically. AD, DS, and DSAD brains also have reduced mtDNA ND6 mRNA levels, altered mtDNA copy number, and perturbed Abeta metabolism. Classical AD genetic changes incorporated into the 3XTg-AD (APP, Tau, PS1) mouse result in reduced forebrain size, life-long reduced mitochondrial respiration in 3XTg-AD males, and initially elevated respiration and complex I and IV activities in 3XTg-AD females which markedly declines with age. **GENERAL SIGNIFICANCE:** Therefore, mitochondrial dysfunction provides a unifying genetic and pathophysiology explanation for AD, PD, and other neurodegenerative diseases. This article is part of a Special Issue entitled Biochemistry of Mitochondria.

---

**Source URL:** <http://www.cirm.ca.gov/about-cirm/publications/mitochondrial-etiology-alzheimer-and-parkinson-disease>